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(57) Abstract

Disclosed are compositions and methods for inhibiting the uptake of proteins and reducing the formation of lysozyme deposits on the outer surface and inner bulk matrix of hydrophilic contact lenses. The method comprises contacting a contact lens with a chemical agent selected from the group consisting of aprotinin, aprotinin derivatives and combinations thereof.

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COMPOSITIONS AND METHODS FOR INHIBITING AND REDUCING LYSOZYME DEPOSITION ON HYDROPHILIC CONTACT LENSES

Field of the Invention

This invention relates generally to cleaning contact lenses. More particularly, the present invention relates to compositions and methods useful for inhibiting the uptake of proteins and reducing the formation of protein deposits on the outer surface and/or in the inner bulk matrix of hydrophilic contact lenses.

Background of the Invention

During handling and wear, contact lenses are susceptible to the accumulation of a variety of materials which may adhere to the surface of the lens and/or lodge within and adhere both chemically and/or spatially to the inner bulk matrix of the lens. For example, during wear, lenses contact proteinaceous materials such as lysozyme and mucoproteins, both of which are constituents of lachrymal tears, and lipids such as sterols, waxes, glycerides, phospholipids, fatty alcohols and acids.

If contact lenses are not properly cleaned, lysozyme, mucoproteins and other soils can accumulate on and/or in the lens to a point where the lens wearer begins to feel discomfort, the lens spectral characteristics are adversely affected, disinfection becomes difficult and/or the gas permeability may be decreased.

Certain types of cleaning or disinfecting techniques and compositions have been found inadequate for inhibiting and reducing the formation of these deposits on hydrophilic contact lenses. For example, it has been shown that sterilization techniques such as heat in the form of boiling water or steam can have adverse effects on soft lenses. High temperatures may cause tear proteins to be baked onto the contact lens polymer, resulting in difficulties in cleaning. Heat sterilization techniques also tend to accelerate lens buildup by precipitating absorbed proteinaceous materials. Sterile saline solutions have limited effect on the removal of soils, thus, requiring some additional cleaning procedure. Peroxides, which are effective disinfectants against ocular

pathogens, have also been found to be inadequate for removing lens soils.

Attempts have been made to reduce and inhibit the tendency for proteins to adhere to a lens surface. For example, U.S. Patent No. 4,168,112 to Ellis discloses forming a thin ionic polymeric coating on a contact lens having an ionically charged surface. The coating is electrostatically bound to the lens surface and reduces the tendency for mucoproteins to adhere to the lens surface. Ellis shows contact lens solutions containing cationic polymers for forming a hydrophilic polyelectrolytic complex on the lens surface wherein the complex acts as a hydrogel "cushion." Other additives to the lens solutions shown by Ellis include preservatives such as ethylenediaminetetraacetic acid (EDTA).

U.S. Patent No. 4,414,127 to Fu discloses compositions which degrade and remove proteinaceous deposits from all types of contact lens plastics by chemically degrading these deposits into water-soluble proteins. Fu shows using metal chloride salts as catalysts for peroxide decomposition where the peroxide is used in a contact lens cleaning solution.

U.S. Patent No. 4,259,202 to Tanaka discloses a solution used for cleaning and preserving contact lenses. The solution of Tanaka contains as an effective ingredient a particular monoester of saccharose with a fatty acid. The solution also contains an alkali metal salt of a saturated fatty acid and a compound selected from the group consisting of a polysaccharide and a polysaccharide derivative. Examples of the polysaccharide and its derivative include alkali metal salt of alginic acid, xanthan gum, alkali metal salt of carboxymethyl cellulose, hydroxypropyl methylcellulose and alkali metal salt of chondroitin sulfuric acid.

Bendazac lysine, an anti-cataract drug, has been found to limit protein deposition on soft contact lenses. See Missiroli, A., Ricci, F., Pocobelli, A., Cedrone, C., Cerulli, L., <u>CLAO Journal (Contact Lens Association of Ophthalmologists)</u>, April 1991, 17(2) pp. 126-8. Bendazac lysine is an oxyacetic acid with known anti-inflammatory, antinecrotic, choleretic and antilipidaemic properties, but it is said that its principal effect is to inhibit the denaturation of proteins.

There continues to be a need for a system capable of effectively reducing, inhibiting and reversing the deposition of proteins, not only from the surface of a contact lens, but also from the inner bulk matrix of the lens. The

accumulation of these proteins in the inner bulk matrix may cause discomfort to the wearer, adversely affect the lens spectral characteristics, decrease lens oxygen permeability and decrease the overall estimated useful lifetime of the lens.

Summary of the Preferred Embodiments

The present invention is directed to ophthalmically safe compositions and methods for cleaning contact lenses, and more specifically to compositions and methods used as in-the-eye and/or out-of-eye inhibitors and reversers of surface and/or inner bulk matrix deposition of lysozyme on hydrophilic contact lenses.

In one aspect of the present invention, the formation of protein deposits on the surface and/or in the inner bulk matrix is reduced and/or inhibited by contacting a contact lens with a solution including an effective amount of a chemical agent selected from the group consisting of aprotinin, aprotinin derivatives and combinations thereof.

In another aspect, the present invention is directed to a method of inhibiting the uptake of proteins and reversing the formation of protein deposits on hydrophilic contact lenses. The method comprises the steps of placing a contact lens in a hypotonic solution for a period of time sufficient to cause the lens to swell and the pores of the matrix to expand. Subsequently, a chemical agent selected from the group consisting of aprotinin, aprotinin derivatives and combinations thereof is added to the solution in an amount sufficient to change the tonicity of the solution in order to cause the lens and the pores to constrict, while also facilitating desorption of protein deposits from the surface and matrix of the lens. The lens is soaked in the solution having the chemical agent for a period of time sufficient to substantially reduce and/or inhibit the formation of protein deposits on and/or in the lens.

The foregoing and other objects, features and advantages of the present invention will become more readily apparent from the following detailed description.

Description of the Preferred Embodiments

The present invention is directed to the use of various chemical agents as in-the-eye and/or out-of-eye inhibitors and reversers of surface and inner bulk

matrix deposition of lysozyme on hydrophilic contact lenses. The present invention is also directed to methods for inhibiting and/or reducing the formation of protein deposits on the surface and/or in the matrix of hydrophilic contact lenses.

While the present invention can be used in connection with a variety of contact lenses, it is preferred that the contact lenses used with the present invention are hydrophilic lenses comprising methacrylic acid as a copolymer. F.D.A. Group III and Group IV lenses are examples of such lenses.

Related methods are disclosed in U.S. Patent Application Serial No. 07/986,959, filed December 9, 1992, which is incorporated in its entirety herein by reference.

In one embodiment, the present invention involves a method of inhibiting the uptake of proteins and/or appreciably reducing the formation of tear protein deposits on the outer surface and/or in the inner bulk matrix of a hydrophilic contact lens. This method comprises contacting a contact lens with a chemical agent selected from the group consisting of aprotinin, aprotinin derivatives and combinations thereof.

For purposes of this invention the term "appreciably" generally means that the lens is more comfortable to the lens wearer and the amount of proteins adhering to the lens is noticeably decreased with the assistance of a 10x magnifier, or with another suitable technique for measuring total lens protein. More specifically, appreciably means the amount of proteins deposited on the lens is preferably reduced by about 40%, more preferably about 40% to about 75%, and even more preferably about 75% to about 95%.

Aprotinin, also known as pancreatic trypsin inhibitor, is a single chain polypeptide comprising 58 amino acids having the following sequence:

Arg Pro Asp Phe Cys Leu Glu Pro Pro Tyr
Thr Gly Pro Cys Lys Ala Arg Ile Ile Arg
Tyr Phe Tyr Asn Ala Lys Ala Gly Leu Cys
Gln Thr Phe Val Tyr Gly Gly Cys Arg Ala
Lys Arg Asn Asn Phe Lys Ser Ala Glu Asp
Cys Met Arg Thr Cys Gly Gly Ala.

Aprotinin inhibits various enzymes in addition to trypsin, including plasmin, chymotrypsin and certain intracellular proteases. Additional properties of

aprotinin are described in The Merck Index, 11th ed., p. 119, entry no. 784 (Merck & Co. 1989), which is incorporated herein by reference.

Aprotinin can be obtained commercially from Bayer under the tradename Trasylol.

For purposes of this aspect of the present invention, aprotinin derivatives are defined as naturally occurring or synthetic (including recombinant) polypeptides in which at least one of the amino acids of sequence I is deleted or replaced with one or more different amino acids. The deletion/replacement does not significantly affect the ability of the molecule to inhibit protein adsorption or absorption to a contact lens while retaining ocular non-toxicicity. Ideally, aprotinin derivatives also retain enzymatic inhibitory activity. Aprotinin derivatives also include aprotinin molecules having one or more substituent groups, including additional N-terminal or C-terminal amino acids, which do not significantly affect the performance of the molecule as indicated above. Aprotinin derivatives which can be used according to the invention include, for example, the recombinant aprotinin "variants" described in U.S. Patent No. 5,231,010, to Ebbers et al., the disclosure of which is incorporated herein by reference. Aprotinin and its derivatives within the scope of the present invention are positively charged at physiological pH's of 7 to 7.4.

Aprotinin and its derivatives are of a size small enough and of optimum steric structure when dissolved in the medium to enter and accumulate in the polymeric pores of the lens bulk matrix such that the ionic charges in the lens will be substantially neutralized at equilibrium as a result of the positively charged agent forming ion pairs with the negatively charged ions of the lens.

It is also possible that an aprotinin or aprotinin derivative precursor could be employed according to the present invention. The precursor can be employed in a form (such as a solid) wherein it is not of the proper size or steric structure, yet when the precursor agent is delivered to the working solution it disassociates or changes sterically in its tertiary or quaternary structure into aprotinin or the desired aprotinin derivative.

The chemical agent (i.e., aprotinin, aprotinin derivatives and/or mixtures thereof) according to the present invention absorbs more rapidly and/or less reversibly into the lens matrix than lysozyme. Thus, the lysozyme which penetrates and adheres to the matrix is displaced by the chemical agent and/or is prevented from accumulating on the lens matrix and surface after the

treatment process and during the lens wear period.

Preferably the chemical agent is dissolved in an aqueous working solution at a pH ranging from about 6 to about 8.5. More preferably, the chemical agent is dissolved in the solution at pH of 7.4.

The solution of the present invention may be a buffered saline solution, contact lens disinfection solution or some other appropriate vehicle which is biocompatible with the eye or is rendered so by the end of the regimen time period. In addition to the chemical agent, the solution of the present invention may also include ophthalmically acceptable additives such as electrolytes, buffers, preservatives, wetting agents, lubricating agents and/or surfactants, all of which are well known in the art. Further, the solution of the present invention may include disinfecting agents. Examples of disinfecting agents which may be used include, but are not limited to, polyquaternary amines, e.g., Croquat™ L which is commercially available from Croda, Inc., biguanides, and polymeric biguanides such as polyhexamethylene biguanide, available as Cosmocil® CQ from ICI Americas, peroxide and water soluble cationic polymers (WSCPs). WSCPs are available from Buckman Laboratories, Inc. and are described in U.S. Patent No. 4,250,269, which is incorporated herein by this reference. Therefore, the solution can be preserved as a soaking solution or as part of a disinfecting solution.

Moreover, the chemical agent can be delivered in a variety of forms including tablet, powder, granules, solution or spray. Such delivery vehicles may contain other ingredients well known in the art so long as they do not affect the chemical agent's function. Such additives include those previously noted as well as fillers, effervescents, biocides and other antimicrobial agents.

Preferably, the lens is contacted with the solution for a period of time such that equilibrium favors desorption of the lysozyme. The desorbed lysozyme is then found solvated in the working solution.

The amount or presence of protein deposits on the lens surface and/or in the lens matrix can oftentimes be determined visually (naturally or with the aid of a magnifying glass) and by the degree of comfort experienced by one wearing the lens. UV spectroscopy or visible light microscopy may also be used to more accurately determine how much protein has been deposited on and in the lens. Chemical assays can also be performed to determine the total amount of protein on and in a contact lens if the lens will not be worn again

and the purpose is solely to use these destructive techniques to measure total protein. Total protein can be chemically assayed utilizing standard techniques such as the ninhydrin assay.

It is preferable to soak the lens in about 2.0 to about 20.0 mL of the solution of the present invention for at least about ten minutes, and more preferably from about ten minutes to about six hours. It should be recognized that the amount of time the lens is to be soaked is inversely proportional to the concentration of the chemical agent contained in the solution. For example, by increasing the concentration of the chemical agent in the solution, the soaking time of the lens will be decreased. The soaking time may also depend upon the particular chemical agent being used and the type of lens being soaked.

Generally, the magnitude of the concentration of the chemical agent and the soak time will depend upon, in addition to the molecular weight of said chemical agent, the amount of lysozyme sorption (adsorption and/or absorption) and the degree of lysozyme attraction to the lens material, as well as the recommended regimen for the user's lenses. It is possible that it may be necessary for the soaking to be repeated several times until the amount and/or the rate of accumulation of lysozyme on and/or in the lens has been appreciably reduced.

Preferably the solution of the present invention contains an effective amount of the chemical agent, i.e., an amount effective to substantially reduce the presence and/or the formation and accumulation of protein deposits on and/or in the lens after a recommended regimen.

More specifically, it is preferred that the working solution contain about 0.01% to about 5.0% by weight of the chemical agent. More preferably, the solution of the present invention contains about 0.1% to about 1.0% by weight of the chemical agent.

It is preferred to soak the lens in the solution at room temperature. Although it may be possible to gently heat the solution, if the solution is more strongly heated, it is possible that the lysozyme may denature and eventually adhere to the lens even more strongly than before the treatment.

It is also preferable that the solution of a chemical agent of the present invention be used to pretreat new contact lenses, that is, lenses that have never been worn before. For example, a contact lens may be prepackaged in the solution. Pretreating a contact lens in this solution will preferably allow the

chemical agent to be sorbed by the lens, including in the lens matrix, such that the [lens/agent] complex is favored in the environment where the lens is exposed to lysozyme, e.g., in the eye. As a result, when the contact lens is first placed in the eye, the lysozyme in the eye will preferably have fewer sites to which to bind.

A lens swelling treatment may be performed in order to reduce the amount of proteins that may adhere to the lens surface and matrix. By making the solution of the present invention hypotonic and contacting the lens in this solution, the lens will appreciably swell and the pores of the matrix will expand, thereby accelerating and facilitating the rate at which the chemical agent binds to the negatively charged sites of the lens. The lens should not be excessively swelled since excessive swelling may permanently damage the lens and may cause the lysozyme to migrate deeper into the small polymeric pores of the matrix. Such a hypotonic solution may be formed, for example, by contacting the chemical agent of this embodiment with water. It is preferable that the hypotonic solution contain 0.0% to about 0.6% and more preferably 0.4% by weight NaCl.

Instead of soaking the lens in the solution of the present invention, the solution may be sprayed, dropped or rubbed directly onto the surface of the lens before the lens is placed on the eye. By using this method of contacting the solution with the lens, it is preferable but not necessary to subsequently rinse the lens with an ophthalmically acceptable rinse solution. Instead, the tear itself will help wash away lysozyme which has been desorbed from the lens.

If the solution is to be contacted with the lens while the lens is in the eye, it is preferable that the solution does not contain more than the isotonic equivalent of the chemical agent, that is, not more than the amount of chemical agent which will produce an isotonic solution of about 290 mOsm/kg tonicity. The upper limit on concentration will also be established by the safe ocular concentration of the particular chemical agent. If the solution should contain less than about 0.1% by weight of the chemical agent, the process of neutralizing the charge of the lens, generally, may take too long or may not be effective at all. On the other hand, if the lens has a low ionicity, it may be possible to effectively neutralize the charge of the lens by soaking it in a solution containing less than 0.1% by weight of the chemical agent.

Use of a chemical agent selected from aprotinin, its derivatives and combinations thereof in accordance with the present invention affords additional advantages. Aprotinin, by virtue of its action in inhibiting a variety of proteolytic enzymes, including proteolytic enzymes in the tear film which can degrade the ocular surface, will prevent this degradation from occurring. Degradation of the ocular surface can lead to breakdown of ocular barrier function and ocular infection. Additionally, ocular pathogens such as *Pseudomonas aeruginosa* produce several proteases, among them elastase and alkaline protease. These have been shown to be important factors in both the establishment of a bacterial infection and the amount of damage caused by the infection to the cornea. Aprotinin can inhibit bacterial-derived enzymes such as those from *Pseudomonas*.

In sum, contacting a contact lens with a chemical agent of the present invention neutralizes the negatively charged ions of the lens material. As a result of this electrostatic interaction, the electrostatic interaction between the lysozyme and the lens material is preferably substantially reduced and/or completely eliminated, thus lowering the primary interactive force responsible for incipient deposition of lysozyme on and/or in the lens.

Lysozyme is the major tear constituent involved in the formation of deposits and lens soils on hydrophilic contact lenses, especially Group III lenses (low water/ionic lens polymers) and Group IV (high water/ionic lens polymers) lenses. Since lysozyme is positively charged at physiological pH and at pHs encountered with lens care products (pH about 7.0 to 8.0), and contact lenses containing methacrylic acid as a copolymer, i.e., Group III and Group IV lenses, are negatively charged under these same conditions, there is formed an electrostatic attraction between the lens material and the lysozyme. With reference to the following equilibria, the typical electrostatic attraction between the lens material and the lysozyme favors an equilibrium of higher concentration of the protein on the lens than in a medium such as a tear or lens care solution and, thus, results in the formation and accumulation of lysozyme on and/or in the lens.

$$\underset{\text{Complex}}{[\text{Lysozyme/Lens}]} \underset{k_C}{\overset{k_{FL}}{\rightleftharpoons}} \text{Lysozyme (solvated) \& Lens-free Lysozyme}$$

$$k_C > k_{FL}$$

For example, Group IV lens materials have a pore size sufficient to accommodate the intrusion and accumulation of lysozyme within the lens. Even though the deeper migration of lysozyme into the lens bulk matrix is a slower process than surface accumulation, protein deposits imbedded in the matrix of a lens are less reversibly bound and are more difficult to remove than proteins deposited on the surface of the lens.

By using a chemical agent according to the present invention to increase k_{FL}/k_C, the solution of the present invention becomes more effective at facilitating inhibiting the uptake of lysozyme and reducing the formation of lysozyme deposits on and in the lens

In another embodiment of the present invention, the chemical agent can be employed alone in combination with one or more additional chemical agents preferably selected from the group consisting of basic polymeric carbohydrates, such as chitosan, chitosan salts such as chitosan hydrochloride, chitosan derivatives such as chitosan biguanide and mixtures thereof.

Chitosan is made by the partial deacetylation of chitin, a polysaccharide obtained from certain fungi and the exoskeletons of arthropods. Chitosan is chemically identical to modified cellulose in which the C-2 hydroxyl groups have been replaced with primary amine functions. This molecule is positively charged at physiological pH's of 7 to 7.4

Preferably, the additional chemical agent possesses a molecular weight ranging from about 100 to about 70,000. More preferably, the additional chemical agent should have a molecular weight and steric structure that is optimum for penetrating the pores. For example, the additional chemical agent should have a molecular weight of not less than about 100 in order to penetrate the pores of the lens more easily and have sufficient charge density to neutralize the charges of the lens more quickly. Conversely, if the chemical agent has a molecular weight greater than 70,000, it may be too large to enter the pores of the lens matrix and neutralize the charge of the lens.

If the chemical agent is only slightly smaller than the pore size of the lens polymers, the lens must be soaked for a longer period of time in order for the chemical agent to neutralize the charge associated with the lens. Desorption of such chemical agents will be slow due to the reduced degrees of freedom in the matrix pore, prolonging the time period of effective prevention of deposition of tear proteins. Thus, an optimum molecular weight between 100 and 70,000 exists for each candidate chemical entity that constitutes a compromise of shortest possible treatment time and longest possible time of effective prevention of protein deposition.

In another embodiment of the present invention, the chemical agent can be added to the hypotonic solution. In this embodiment, the chemical agent preferably has a delayed or time-release coating. This allows more time for the lens to swell and facilitate the rate at which the agent binds to the negatively charged sites of the lens, before the lens and the pores of the matrix shrink back to their previous, desired size prior to having been placed in the hypotonic solution.

Even though the chemical agent of this embodiment may be directly added to the hypotonic solution in the form of a solution, in order to add the chemical agent to the hypotonic solution in a delayed-release manner it is preferred that the chemical agent be present in the form of a tablet, pill, capsule, powder or the like which includes a coated portion. For example, a tablet may have a core containing the chemical agent and thereupon placed a barrier component coating to delay release of the chemical agent present in the core.

If the solution to which the agent is added has a pH higher or lower than physiological pH, it may be desirable to add an additive to the core in order to maintain and/or bring the pH of the working solution to about 7.0 to about 8.0. Lysine dihydrochloride, tartaric acid, citric acid, sodium carbonate and mixtures thereof are examples of additives which may be used to help adjust the pH of the solution.

The barrier component coating can act to delay the release of the chemical agent from the core portion, preferably, for a period of time sufficient to reduce the accumulation of lysozyme at the surface of the lens and in the lens matrix.

The delayed-release of the chemical agent into the solution may be

accomplished in any one of a number of suitable ways, a number of which are conventional and well known in the art. A barrier component may consist of a slowly dissolving coating material.

Barrier components suitable as coatings include water soluble vinyl polymers such as polyvinyl pyrrolidone, polyvinyl alcohol and polyethylene glycol; water soluble protein, polysaccharide and cellulose derivatives such as methylcellulose, hydroxypropyl methylcellulose, sodium carboxymethylcellulose, alginic acid and its salts and other derivatives, and the like and mixtures thereof.

The amount of barrier component used is not critical in the present invention provided that such barrier component functions as described herein.

A preferred delayed-release coating or barrier component is derived from a mixture comprising polyvinyl alcohol and a water soluble soaking component.

Alternatively, instead of providing a tablet, for example, having a core containing the chemical agent, the core may include only the pH adjusting additive, and the additive may be covered with a mixture of the chemical agent and the barrier component. Also, the tablet may be comprised of a core which includes the pH adjusting additive. This core may then be covered with the barrier component, and the barrier component, in turn, may be covered by the chemical agent which is also covered with another layer of the barrier component.

Exemplary compositions for use according to the present invention are given below. All amounts are in weight percent.

<u>Example 1</u>	Buffered saline solution
Disodium EDTA	0.10 w/v %
Sodium chloride	0.85
Boric acid	0.10
Aprotinin	0.10
1 N NaOH	to adjust to pH 8.0
Water	balance

<u>Example 2</u>	Soft lens cleaner
Miranol 2MCA, modified	0.002 w/v %
Sorbic acid	0.110

EDTA	0.20
Propylene glycol	0.0011
Hydroxyethyl cellulose	0.50
Aprotinin	0.10
Water	balance

Lenses to be cleaned are rubbed with 3 drops for 20 seconds as part of a cleaning regimen including heat treatment.

Example 3 Multipurpose solution

Polyhexamethylene biguanide, Cosmocil CQ	0.0001 w/v %
Edetate disodium USP	0.05
Sodium chloride USP	0.37
Tromethamine	1.20
Tyloxapol USP	0.025
Aprotinin	0.10
HCl	to adjust to pH 7.5
Water	balance

Example 4 Multipurpose solution

Hydroxyethyl cellulose NF	0.65 w/v %
Sodium chloride USP	0.67
Boric acid NF	0.39
Sodium borate decahydrate NF	0.20
Edetate disodium USP	0.127
WSCP	0.006
Croquat L	0.010
Aprotinin	0.10
Water	balance

Example 5	Multipurpose solution
Pluronic F-127	0.10 w/v %
Sodium chloride	0.40
Boric acid	0.39
Sodium borate decahydrate NF	0.20
Edetate disodium	0.100
WSCP	0.003
Aprotinin	0.10
Water	balance

Example 6	Tablet
Di-Pac	40.0 mg/tablet
Polyethylene glycol 3350	4.0
Povidone PVP K-30	4.0
Aprotinin	2.0

Example 7	Tablet
Di-Pac	40.0 mg/tablet
Polyethylene glycol 3350	4.0
Povidone PVP K-30	4.0
Sodium carbonate, anhydrous	2.0
Aprotinin	2.0

Di-Pac is a compressible sugar comprised of 97 w/w % sucrose and 3 w/w % maltodextrin. Di-Pac is commercially available from Amstar Sugar Corp. and is distributed by Austin Chemical Co. of Illinois.

The tablets of Examples 6 and 7 can abe dissolved in contact lens multipurpose solutions. In particular, the tablets can be dissolved in 2.0 ml of a contact lens multipurpose soaking, cleaning, disinfecting and rinsing solution such as ReNu, sold by Bausch and Lomb; Optifree, sold by Alcon; and Complete, sold by Allergan.

Having thus described the exemplary embodiments of the present invention, it should be noted by those skilled in the art that the within disclosures are exemplary only and that various other alternatives, adaptations and modifications may be made without departing from the spirit and scope of the present invention. Accordingly, the present invention is not limited to the specific embodiments illustrated herein, but is only limited by the following claims.

What is claimed is:

1. A method of reducing the formation and inhibiting the uptake of protein deposits on the outer surface and/or in the inner bulk matrix of a hydrophilic contact lens, comprising the step of contacting a contact lens with a chemical agent selected from the group consisting of aprotinin, aprotinin derivatives and combinations thereof.

2. The method as defined in claim 1 wherein said agent is aprotinin.

3. The method as defined in claim 1 wherein the lens is contacted with a solution containing said agent in an amount of about 0.01% to 5.0% by weight.

4. The method as defined in claim 1 further including adding said chemical agent to an aqueous solution wherein said solution has a pH ranging from 6 to 8.

5. The method as defined in claim 4 wherein prior to contacting said lens with said solution, said lens is contacted with a hypotonic solution for a period of time to appreciably swell said lens.

6. The method as defined in claim 1 wherein said chemical agent is employed in combination with at least one additional chemical agent selected from the group consisting of chitosan and its salts and derivatives.

7. A method of reducing the formation and inhibiting the uptake of protein deposits on the outer surface and/or in the inner bulk matrix of a hydrophilic contact lens comprising the step of contacting said contact lens with a solution at physiological pH containing at least 0.05% by weight of a chemical agent selected from the group consisting of aprotinin, aprotinin derivatives and combinations thereof, wherein said solution has a pH ranging from about 6 to about 8.5.

8. The method as defined in claim 7 wherein said solution is hypotonic.

9. A method of reducing the formation and inhibiting the uptake of protein deposits on and/or in a hydrophilic contact lens wherein the lens has an outer surface and an inner bulk matrix with polymeric pores, the method comprising the steps of:

a) placing the lens in a hypotonic solution for a period of time sufficient to cause the lens to swell and the pores of the matrix to expand;

b) adding to the solution a chemical agent selected from the group consisting of aprotinin, aprotinin derivatives and combinations thereof, such that the solution possesses an osmotic pressure sufficient to cause the lens and the pores of the matrix to constrict, and wherein the chemical agent is present in an amount sufficient to cause desorption of the protein deposits from the surface and/or matrix of the lens; and

c) soaking the lens in the solution having the chemical agent for a period of time sufficient to appreciably reduce the formation of protein deposits on or in the lens.

10. The method as defined in claim 9 wherein said chemical agent is aprotinin.

11. The method as defined in claim 9 wherein there is present by weight about 0.01% to 5.0% of said chemical agent.

12. The method as defined in claim 9 further including adding said chemical agent to an aqueous solution wherein said solution has a pH ranging from 6 to 8.

13. The method as defined in claim 9 wherein said chemical agent is employed in combination with at least one additional chemical agent selected from the group consisting of chitosan and its salts and derivatives.

14. For use in a contact lens solution, a composition for reducing the formation and inhibiting the uptake of protein deposits on the outer surface and/or in the inner bulk matrix of a hydrophilic contact lens, said composition comprising an effective amount of a chemical agent selected from the group consisting of aprotinin, aprotinin derivatives and combinations thereof.

15. The composition as defined in claim 14 wherein there is present in the solution about 0.01% to 5.0% by weight of said chemical agent.

INTERNATIONAL SEARCH REPORT

Interr   ial Application No
PCT/US 94/11243

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C11D3/37

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 C11D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	EP,A,0 420 600 (CZECHOSLOVAK ACADEMY OF SCIENCES) 3 April 1991 see claims 1,2,13 ---	1,2,14
A	DATABASE WPI Section Ch, Week 9002, Derwent Publications Ltd., London, GB; Class A96, AN 90-012294 & JP,A,1 293 314 (DAICEL CHEM IND KK) 27 November 1989 see abstract --- -/--	1,6

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
20 February 1995	27.02.95

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Serbetsoglou, A

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INTERNATIONAL SEARCH REPORT

Interr onal Application No
PC1/US 94/11243

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	DATABASE WPI Section Ch, Week 8914, Derwent Publications Ltd., London, GB; Class A96, AN 89-103364 & JP,A,1 050 014 (TOME SANGYO KK) 27 February 1989 see abstract ---	1,6
A	US,A,4 259 202 (TANAKA ET AL.) 31 March 1981 cited in the application see the whole document ---	1,4,5
A	US,A,4 414 127 (FU) 8 November 1983 cited in the application see claim 1 ---	1
P,A	WO,A,94 13774 (ALLERGAN INC.) 23 June 1994 cited in the application -----	1,4-9, 12-14

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INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/US 94/11243

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		CA-A- 2026166	30-03-91
		US-A- 5244673	14-09-93
US-A-4259202	31-03-81	JP-C- 1283418	27-09-85
		JP-A- 55115497	05-09-80
		JP-B- 60008484	04-03-85
US-A-4414127	08-11-83	NONE	
WO-A-9413774	23-06-94	AU-B- 5685094	04-07-94